

Patent claims

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Compounds of the general formula (I)

in which

A, D, E and G are identical or different and represent CH groups or nitrogen atoms,

(I),

L1 and L2 are identical or different and independently of one another each represents one or more radicals selected from the group consisting of hydrogen, halogen, hydroxyl, carboxyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, (C1-C6)-alkyl, (C1-C6)-alkoxy or (C1-C6)-alkoxy-carbonyl,

 R^1 represents the CH_2 -OH group, or represents a radical of the formula CO- NR^4R^5

20 in which

R⁴ and R⁵ are identical or different and each represents hydrogen or (C₁-C₆)-alkyl,

25 R² represents (C₃-C₈)-cycloalkyl,
represents (C₁-C₈)-alkyl which is optionally interrupted by an oxygen
or sulphur atom or by a radial NR⁶,
represents a 4- to 8-membered saturated heterocycle which is attached
to the imidazole ring via a nitrogen atom and which optionally
contains a further oxygen or sulphur atom, or



represents a 4- to 8-membered saturated heterocycle which contains a radical of the formula NR⁷ and optionally additionally one nitrogen, oxygen or sulphur atom,

M (10)

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35 and

where (C₃-C₈)-cycloalkyl, (C₁-C₈)-alkyl which is optionally interrupted by one oxygen or sulphur atom, the 4- to 8-membered saturated heterocycle which is attached to the imidazole ring via a nitrogen atom and which optionally contains one further oxygen or sulphur atom and optionally (C₁-C₈)-alkyl which is interrupted by a radical of the formula NR⁶ and optionally the 4- to 8-membered saturated heterocycle which contains a radical of the formula NR⁷ and optionally additionally one nitrogen, oxygen or sulphur atom are substituted by one to three hydroxyl groups and/or by a radical of the formula -NR⁸R⁹

in which

R⁶ and R⁷ are identical or different and each represents hydrogen, (C₁-C₆)-alkyl, hydroxy-(C₁-C₆)-alkyl or (C₃-C₇)-cycloalkyl,

 R^8 and R^9 are identical or different and each represents hydrogen, $(C_1\text{-}C_6)$ -alkyl or $(C_3\text{-}C_7)$ -cycloalkyl,

or

R⁸ and R⁹ together with the nitrogen atom form a 4- to 8-membered saturated heterocycle which may optionally additionally contain one exygen or sulphur atom or a radical of the formula NR¹⁰

in which

R¹⁰ represents hydrogen, (C₁-C₆)-alkyl or (C₃-C₇)-cycloalkyl

 R^3 represents a phenyl, naphthyl, pyrimidinyl, pyridyl, furyl or thienyl ring, where the rings are optionally mono- or polysubstituted by radicals selected from the group consisting of halogen, hydroxyl, carboxyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, 5 (C_1-C_6) -alkyl, (C_1-C_6) -alkoxy or (C_1-C_6) -alkoxycarbonyl, and their salts. Compounds according to Claim 1 where A, D, E and G each represent the CH group, 15 or one of the radicals A, D, H and G represents a nitrogen atom and the others each represent the CH group, L1 and L2 are identical or different and independently of one another each represents one or more radicals selected from the group consisting of 20 hydrogen, fluorine, chlorine, cyano, trifluoromethyl or trifluoromethoxy, R^1 represents the -CH₂-ΦH group, or represents a radical of the formula -CO-NR⁴R⁵ 25 in which R⁴ and R⁵ are identical or different and each represents hydrogen or (C_1-C_3) -alkyl, 30 R^2 represents (C₃-C₇)-cycloalkyl, represents (C₁-C₆)-alkyl which is optionally interrupted by an oxygen or sulphur atom or by a radical NR⁶, represents a 5- to 7-membered saturated heterocycle which is attached 35 to the imidazole ring via a nitrogen atom and which optionally contains a further oxygen or sulphur atom, or

represents a 5- to 7-membered saturated heterocycle which contains a radical of the formula NR⁷ and optionally additionally one nitrogen, oxygen or sulphur atom,

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15 (Sr)

where (C₃-C₇)-cycloalkyl, (C₁-C₆)-alkyl which is optionally interrupted by one oxygen or sulphur atom, the 5- to 7-membered saturated heterocycle which is attached to the imidazole ring via a nitrogen atom and which optionally contains one further oxygen or sulphur atom and optionally (C₁-C₆)-alkyl which is interrupted by a radical of the formula NR⁶ and optionally the 5- to 7-membered saturated heterocycle which contains a radical of the formula NR⁷ and optionally additionally one nitrogen, oxygen or sulphur atom are substituted by one to three hydroxyl groups and/or by a radical of the formula -NR⁸R⁹

in which

 R^6 and R^7 are identical or different and each represents hydrogen, (C_1-C_4) -alkyl, hydroxy- (C_1-C_4) -alkyl or (C_3-C_6) -cycloalkyl,

R⁸ and R⁹ are identical or different and each represents hydrogen, (C₁-C₄)-alkyl or (C₃-C₆)-cycloalkyl,

or

R⁸ and R⁹ together with the nitrogen atom form a 5- to 7-membered saturated heterocycle which may optionally additionally contain one oxygen or sulphur atom or a radical of the formula NR¹⁰

in which

R¹⁰ represents hydrogen, (C₁-C₄)-alkyl or (C₃-C₆)-cycloalkyl

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represents a phenyl, pyridyl or thienyl ring which is optionally mono- \mathbb{R}^3 or polysubstituted by radicals selected from the group consisting of fluorine, chlorine, cyano, trifluoromethyl or trifluoromethoxy, and their salts. 3. where 10 15 R^1 in which 20 R^2

Compounds according to Claim 1 A, D and E each represent a CH group, G represents a nitrogen atom or represents a CH group, L¹ and L² each represent hydrogen, represents a radical of the formula -CO-NR⁴R⁵, R⁴ and R⁵ each represent hydrogen, represents (C₁-C₄)-alkyl which is optionally interrupted by one oxygen atom, or represents a 4-R⁷-piperazin-1-yl radical 25 where (C₁-C₄)-alkyl which is optionally interrupted by one oxygen atom is substituted by a hydroxyl group or by a radical of the formula -NR⁸R⁹ 30 in which R⁷ represents hydrogen, (C₁-C₄)-alkyl or (C₃-C₆)-cycloalkyl, R⁸ and R⁹ are identical or different and each represents hydrogen, 35

 (C_1-C_4) -alkyl or (C_3-C_6) -cycloalkyl,

5 and

R³ represents a phenyl radical,

and their salts.

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4. (S)-N- $\{\{(1R, 2R)-2-\{4-\{[2-(4-Methyl-piperazin-1-yl)-benzimidazol-1-yl]methyl\}-phenyl\}-cyclohex-1-yl\}carbonyl}-phenylglycinamide$

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and its salts.

5. Process for preparing compounds of the general formula (I) according to Claims 1 to 4, characterized in that

[A] compounds of the general formula (II)

$$\bigcup_{L^2} O - T$$
 (II).

in which

L² is as defined in Claim

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T represents (C_1-C_4) -alkyl, preferably methyl or tert-butyl,

and

$$R^{11}$$
 $A D$
 $G \stackrel{E}{=} L^{1}$
(III),

in which

A, D, E, G and L¹ are each as defined in Claim 1

and

R¹¹ has the meaning of R² given in Claim 1, where amino and hydroxyl functions are optionally blocked by suitable amino or hydroxyl protective groups,

in inert solvents, depending on the definition of R¹¹ optionally in the presence of a base, into the compounds of the general formula (IV)

$$R^{11}$$
 N
 $G = E$
 CO_2-T
 L^2
 $(IV),$

in which

R¹¹, A, D, E, G, L¹, L² and t are each as defined above,

which are converted in a subsequent step using acids or bases into the corresponding carboxylic acids of the general formula (V)

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$$R^{11}$$
 CO_2H
 CO_2H
 CO_2H

in which

R¹¹, A, D, E, G, L¹ and L² are each as defined above,

which are subsequently reacted by known methods with compounds of the general formula (VI)

(VI),

in which

R¹ and R³ are each as defined in Claim 1

in inert solvents,

and, if R11 carries one of the abovementioned protective groups, these are optionally removed by customary methods either in the hydrolysis to the acids (IV) -> (V) of after the reaction with the compounds of the general formula (VI),

20 or

> [B] if R² represents a saturated heterocycle which is attached directly via a nitrogen atom to the imidazole ring,

> the abovementioned compounds of the general formula (II) are initially converted with compounds of the general formula (IIIa)

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Y-N-D-L1

(IIIa),

in which

A, D, E, G and L¹ are each as defined in Claim 1

and

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Y represents halogen or mesyl, preferably chlorine, bromine or mesyl,

in inert solvents into the corresponding compounds of the formula (VII)

Y
$$CO_2$$
-T CO_2 -T CO_2 -T CO_3 -T

in which

Y, A, D, E, G, L¹, L² and T are each as defined above,

which are reacted in a subsequent step with compounds of the general formula (VIII)

 $HNR^{12}R^{13}$ (VIII)

in which

R¹² and R¹³ together with the nitrogen atom form a heterocycle according to the definition of R²

25 to give compounds of the general formula (IX)

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$$R^{12}R^{13}N$$
 $G = E$
 CO_2 -T
 L^2
 (IX) ,

in which

A, D, E, G, L¹, L², R¹², R¹³ and T are each as defined above,

which are, in the subsequent steps, converted as described under [A] by hydrolysis into the corresponding carboxylic acids of the general formula (X)

$$R^{12}R^{13}N$$
 $R^{12}R^{13}N$
 $R^{12}R^{13}$

in which

A, D, E, G, L^1 , L^2 , $R^{1/2}$ and $R^{1/3}$ are each as defined above,

and these compounds are subsequently reacted with the compounds of the general formula (VI) according to known methods for preparing amides from carboxylic acids and amines and, if appropriate, converted into the corresponding salts by reaction with an acid.

6. Compounds of the general formula (IV)

in which

A, D, E, G, L¹, L², R¹¹ and T are each as defined in Claims 1 and 5

and their salts.

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7. Compounds of the general formula (V)

$$R^{11}$$
 $G = E$
 CO_2H
 CO_2H
 CO_2H
 CO_2H

in which

A, D, E, G, L^1 , L^2 and R^{11} are each as defined in Claims 1 and 5

and their salts.

8. Compounds of the general formula (VII)

in which

A, D, E, G, L¹, L², Y and T are each as defined in Claims 1 and 5

and their salts.

9. Compounds of the general formula (IX)

$$R^{12}R^{13}N$$
 N
 $G = E$
 CO_2-T
 CO_2-T
 CO_2

in which

A, D, E, G, L¹, L², R¹², R¹³ and T are each as defined in Claims 1 and 5

and their salts.

10. Compounds of the general formula (X)

$$R^{12}R^{13}N$$
 N
 G
 E
 CO_2H
 L^2
 (X)

in which

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A, D, E, G, L¹, L², R¹¹ and R¹² are each as defined in Claims 1 and 5

and their salts.

11. Medicaments, comprising a compound of the general formula (I) according to any of Claims 1 to 4 in admixture with at least one pharmaceutically acceptable, essentially non-toxic carrier or excipient.

20 12. Compounds according to any of Claims 1 to 4 for use as medicament in the treatment of humans and animals.

13. Use of compounds according to any of Claims 1 to 4 for preparing medicaments for the treatment and/or prophylaxis of ischaemic brain disorders.

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14. Use of compounds according to any of Claims 1 to 4 for preparing medicaments for the treatment and/or prophylaxis of stroke, reperfusion damage or brain trauma.

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